Cont.

22. A substantially detoxified mutant according to claim 19, wherein said mutant is a mutant of whole *Bordetella pertussis* toxin.--

**REMARKS**

Claims 2-10 have been pending and, among these, nonelected claims 2-4 were withdrawn and claims 5-10 were rejected under 35 USC §112. In the present response, claims 2-10 have been canceled and new claims 11-22 are added. Thus, claims 11-22 are pending for reexamination and reconsideration, which are respectfully requested in view of the following remarks. Further, for the reasons discussed below, applicant also requests declaration of an interference between this application, a patent, and two or more additional applications.

On pages 2-4 of the Official Action, the specification was objected to, and claims 5-10 were rejected, under the first paragraph of 35 USC §112, for an alleged failure to provide an "enabling" disclosure. The examiner identified two grounds for the rejection. First, the examiner contends that the specification fails to reveal any mutants with enzymatic activity that is "substantially reduced," *i.e.*, 1000-fold less than or negligible compared to wild type *Bordetella pertussis* toxin. (Action at page 2.) Second, the examiner believes that it would require "undue" experimentation to extend the claims to include mutations other than those at position 9, and that applicant has provided no guidelines for predicting success with any sequence encoding less than the entire carboxy terminus. This rejection, as it may be applied to new claims 11-22, is respectfully traversed.

As to the phrase "substantially reduced," the application defines this term as

> more than about 1000 fold less enzymatic activity or almost negligible enzyme activity compared to the normal (wild type) activity.

Application at page 47, lines 10-13. The examiner is invited to review Table 6 on the last page of the specification and, in particular, to review the activity for the negative control mutant 20A. The ADP-ribosyltransferase activity of mutant 20A, which was an inclusion body lacking any S1-related proteins, was reported as 839 ± an experimental error of 68. Because negative control 20A cannot possess ADP-ribosyltransferase activity, the value of 839 ± 68 essentially represents zero activity in the assay used. Mutant 4-1, which contained a lysine substituted for the 9 position arginine, exhibited an even lower ADP-ribosyltransferase activity of 754 ± 7. Thus, the activity value for the 4-1 mutant, which was below the value corresponding to zero activity, clearly was negligible and thus well within the range defined as "substantially reduced." The examiner is requested, therefore, to reconsider and withdraw this basis of rejection.

With regard to the second stated basis for the examiner's rejection, applicant respectfully submits that prior-pending claims 2-10, as well as new claims 11-16, are of scope fully commensurate with enablement. The first paragraph of 35 USC 112 requires nothing more than objective enablement; see *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991) and cases cited therein. Accordingly, in making a rejection for lack of enablement, it is incumbent upon the Examiner to explain why the objective truth of the disclosure is doubted and to back up such assertions with acceptable objective evidence or reasoning in support thereof. Only in this manner does an applicant have a fair opportunity to overcome

the Examiner's doubts by submitting suitable proofs to indicate that the specification is indeed enabling. In meeting the enablement requirement a patent need not teach, and preferably omits, what is well known in the art. See 37 CFR §1.71(c); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81, 94 (Fed. Cir. 1986). How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance since a specification which teaches how to make and use the invention in terms which correspond in scope to the claims must be taken as complying with the first paragraph of 35 USC §112 unless there is reason to doubt the objective truth of the statements relied upon therein for enabling support. *In re Vaeck, supra, In re Marzocchi*, 438 F.2d 220, 169 USPQ 367 (CCPA 1977).

This precedent is especially significant in light of the fact that the PTO already has recognized the propriety of claims like those proffered by applicant. The examiner is invited to review the claims of U.S. patent No. 5,085,862 (copy attached as Exhibit 1), which are of similar scope to the claims presently rejected. (As discussed below, an interference with this patent is requested.) For example, claim 1 of the patent recites:

> 1. An immunoprotective genetically detoxified mutant of pertussis holotoxin.

Thus, the PTO already has issued claims of scope similar to those rejected in this case. The examiner is requested, therefore, to reconsider and withdraw this basis of rejection.

In view of the foregoing remarks, the examiner is respectfully requested to reconsider and withdraw the outstanding rejection under Section 112.

The examiner is advised that a petition to amend inventorship shortly will be filed in this application.

**REQUEST FOR INTERFERENCE**

In accordance with 37 CFR §§1.604 and 1.607, applicant hereby requests an interference between this application and the following patent and applications:

1. U.S. Patent No. 5,085,862 to Klein *et al*. ("the '862 patent"), and any pending continuing applications claiming related subject matter;

2. Application Serial No. 07/094,307 filed September 4, 1987 ("the '307 application");

3. Application Serial No. 07/232,482 filed August 17, 1988 ("the '482 application"); and

4. Application Serial No. 07/632,265 filed December 21, 1990 ("the '265 application").

Each of the three identified applications is believed to name Walter Neal Burnette III as the sole inventor. The undersigned is not aware of the exact status of the Burnette applications, such that there may be one or more related continuing applications which should be included in the interference. In an information disclosure statement filed June 3, 1991, applicant previously made the examiner aware of a European patent application, No. 306,318 ("the EPO application") (copy attached as Exhibit 2), which claims priority to the '307 and '482 applications. The undersigned believes that the '265 application may be a continuation of the '307 application and, hence, that the '307 application may be abandoned.

Further, there may be pending continuing applications related to the '862 patent. During prosecution of the application which matured into that patent, there was a restriction requirement which resulted in withdrawal of originally-filed claims 17-26 from consideration. Presumably, therefore, there could be one or more pending divisional applications, as well as one or more continuations and/or continuations-in-part.

Since the claims of the '862 patent recite a mutant protein, the following count directed to a mutant protein is suggested for the interference:

> A substantially detoxified mutant of at least a portion of the S1 subunit of *Bordetella pertussis* toxin, said mutant comprising an epitope that contributes to immunoprotection against *Bordetella pertussis* toxicity.

To facilitate declaration of an interference using the above proposed count, applicant has added new claim 17, which is identical to the proposed count. Dependent claims 18-22, which depend from claim 17, also have been added.

Alternatively, since the involved patent and applications also disclose the DNA encoding such proteins, the following count directed to a DNA instead may be used:

> A DNA molecule encoding a substantially detoxified mutant of at least a portion of the S1 subunit of *Bordetella pertussis* toxin, said mutant comprising an epitope that contributes to immunoprotection against *Bordetella pertussis* toxicity.

Both proposed counts define subject matter common to the interfering applications and patent. The proposed counts, and particularly the proposed count reciting a detoxified mutant, while similar to the issued claims of the '862 patent, are broader and, therefore, are proper under 37

CFR §1.606. The proposed counts are broader because they are not directed exclusively to "holotoxins" (whole toxins) as recited in claim 1 of the '862 patent, but also embrace mutants of at least a portion of the S1 subunit of *Bordetella pertussis* toxin. The S1 subunit is the subunit of *pertussis* toxin responsible for both its toxicity and immunogenicity, and all of the parties to the proposed interference achieved detoxified mutants by mutating the S1 subunit.

That such a count would be proper is further evidenced by the proposed designation of corresponding claims. Specifically, claims 11-22 of this application would correspond to the count, as would claims 1 and 3-16 of the '862 patent. (Claim 2 of the '862 patent is directed to mutants of the B portion of *pertussis* toxin, which does not contain the S1 subunit, and thus claim 2 would not correspond to the count.) It is not known precisely which claims of the Burnette applications would correspond to the count.

The proposed counts also are proper, moreover, in that they correspond to the best proofs of the applicant.

Applicant hereby petitions for a three month extension of time to respond to the April 3, 1992 Official Action. A check in the amount of $840.00 for the extension fee is attached. If any additional fees are required, the Commissioner is authorized to charge the necessary fees to Deposit Account No. 19-0741.

The examiner is courteously invited to contact the undersigned should the examiner have any questions which might be resolved over the telephone.

Respectfully submitted,

October 5, 1992
Date

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